LG-4878 REV. 9/89

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Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

8E CAP

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment, See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).

o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.

othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

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[6] 43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112

"Birth Defects" listed.

[14] Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

---

[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

CAS: Not known
Chem: N.N'dimethylhydroxyacetamide
Title: Preliminary Toxicity Tests of Four Derivatives of Dimethylamine
Date: 12/2/55
Summary of Effects: brain hemmorhage

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HL-0074-55
MR-0048-007

Haskell Laboratory for Toxicology and Industrial Medicine
Employee Relations Department
E. I. du Pont de Nemours and Co., Inc.
Wilmington, Delaware
December 2, 1955

W. K. Lowen (2)
Grasselli Chemicals Department
Experimental Station

PRELIMINARY TOXICITY TESTS OF FOUR DERIVATIVES OF DIMETHYLAMINE

Medical Research Projects MR-13 and MR-48

On October 16, 1950, A. G. Jelinek submitted four dimethylamine derivatives for preliminary toxicity evaluation. The chemicals are:

Dimethylammonium dimethylcarbamate	TD 1023-47B	H-521
N,N-Dimethylacetamide	TD-1023-47C TD-991-26A	H-519 127-19-5 H-536
N,N-Dimethylhydroxyacetamide	TD-978-36	H-518
N,N-Dimethylallylamine	TD-991-13	H-520 2155-94-4

Dimethylammonium Dimethylcarbamate

Acute Oral Toxicity

The Approximate Lethal Dose (ALD) was determined to be 2250 mg/kg when dimethylammonium dimethylcarbamate was administered by stomach tube to male albino rats in the form of an aqueous solution. Animals receiving lethal doses exhibited discomfort, with labored breathing, and in one instance, cyanosis. The cause of death was diagnosed as acute gastroenteritis. Animals receiving sublethal doses showed no unusual clinical signs, and no evidence of pathological change was found on autopsy.

Subacute Oral Toxicity

When five rats were given repeated doses of 450 mg/kg/day of dimethylammonium dimethylcarbamate, four of the five animals survived the full ten treatments. The other animal was sacrificed after the sixth treatment when it appeared that death was imminent. This animal was found to be suffering from gastritis. The four surviving animals showed no unusual clinical signs except occasional diarrhea during the treatment period. All of them lost weight initially. On autopsy, no pathological changes attributable to the chemical treatment were found.

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Skin Irritancy and Sensitization

In tests on freshly shaven skin of guinea pigs, dimethylammonium dimethylcarbamate was found to be mildly irritating. There seemed to be no difference in the effects on dry or moist skin. Sensitization tests gave negative results.

N,N-Dimethylacetamide

Acute Oral Toxicity

The Approximate Lethal Dose (ALD) by oral administration to rats was 7500 mg/kg. The animal receiving the lethal dose showed discomfort and labored breathing and was dead within twenty-four hours. Autopsy findings did not establish the anatomical cause of death.

The Approximate Lethal Dose (ALD) by oral administration to guinea pigs was found to be 3400 mg/kg. The animals receiving lethal doses were found to have acute gastritis, and this condition was diagnosed as the cause of death. Animals receiving sublethal doses exhibited no pathological changes attributable to the test chemical.

Subacute Oral Toxicity

Six male albino rats were given repeated doses of 1500 mg/kg/day of N,N-dimethylacetamide. Three of the six survived the full program of ten treatments. Two died after five doses, and another after six treatments. During treatment the animals exhibited marked discomfort, irritability, pallor, and loss of weight. Several of the animals suffered from severe diarrhea. At autopsy, pathological changes were found in the kidney, liver and stomach.

Inhalation Toxicity

Two rats were exposed to a concentration averaging about 10 mg/lit for a total exposure time of 48 hours. The rats survived with no obvious clinical signs. At autopsy, no definite pathological change attributable to the test chemical was determined. It was noted, however, that there was some swelling of the cells lining the alveolar walls of the lungs.

Skin Irritancy and Sensitization

N,N-Dimethylacetamide was found to be irritating to intact guinea pig skin when applied as a 25 per cent aqueous solution. With a 10 per cent solution, there was practically no irritation to intact skin, but a temporary moderately irritating effect was produced by the 10 per cent aqueous solution on abraded skin. Tests for sensitization were negative.

Acute Skin Absorption Toxicity

When N,N-dimethylacetamide was applied to the shaved skin of male albino rabbits, the Approximate Lethal Dose (ALD) was found to be 5000 mg/kg.

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There was acute local inflammation of the treated area. On autopsy, a number of pathological changes were noted, including edema and congestion of the kidney, congestion of the thymus and congestion of the blood vessels of the eye. However, no specific anatomical cause of death was demonstrated.

Subacute Skin Absorption Toxicity

Six of six rabbits survived ten treatments of 1000 mg/kg/day of N,N-dimethylacetamide when the undiluted material was applied to the shaved skin. There was a slight initial weight loss in the treated animals, but the rabbits all gained weight during the two weeks of observation following the treatment period. On autopsy at sacrifice, no pathological changes could be determined attributable to the test chemical.

A subacute skin absorption toxicity test was also run using male albino rats. Treatments were made at the rate of 7500 mg/kg/day, and two rats were used. One animal died during the third treatment and the second died after the fourth treatment. Pathological examination showed that there was substantial damage to the liver and bone marrow.

N,N-Dimethylhydroxyacetamide

Acute Oral Toxicity

The Approximate Lethal Dose (ALD) orally for male albino rats was found to be >7500 mg/kg. The test animals showed no unusual clinical signs and the findings at autopsy indicated no pathological changes.

Subacute Oral Toxicity

Six rats were given repeated daily doses of 5000 mg/kg. At the end of four such treatments, four of the rats were dead and the other two were sacrificed after the fifth treatment. The findings at autopsy were consistent with a diagnosis of central nervous system stimulation. The meningeal vessels of the brain were slightly congested, and there was evidence of hemorrhaging.

Six other rats were treated with daily doses of 1500 mg/kg; all six survived 15 such treatments. The findings at autopsy showed no pathological changes attributable to the test chemical.

Skin Irritancy and Sensitization

When N,N-dimethylhydroxyacetamide was applied as a 50 per cent aqueous solution to intact guinea pig skin, a mild temporary irritation was produced. Tests for sensitization were negative.

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N,N-Dimethylallylamine

Acute Oral Toxicity

The Approximate Lethal Dose (ALD) was determined to be 1000 mg/kg when the dimethylallylamine was administered by stomach tube to male albino rats. Animals receiving lethal doses exhibited discomfort and labored breathing. Gastroenteritis was the principal finding on autopsy. Some injury to the stomach occurred even at the lowest non-lethal dose tested, 100 mg/kg.

Subacute Oral Toxicity

Six of six rats survived ten treatments of 200 mg/kg/day of N,N-dimethylallylamine. No unusual clinical signs were noted. However, on sacrifice and autopsy, gastritis was diagnosed in each of the test animals.

Skin Irritancy and Sensitization

N,N-Dimethylallylamine was found to be very mildly irritating to both intact and abraded skin of guinea pigs when tested as a 50 per cent aqueous solution. There was no evidence of sensitization from this chemical.

Jonathan W. Williams
Assistant Director

JWW:ecd
12/2/55
Report No. 74-55

Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP CAP

Submission number: 13151A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

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entire document: 0 1 2 **pages** 1, 1st tab **pages** [redacted]

Notes:

Contractor reviewer : LPS **Date:** 12/6/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA/ Submission # SEND: 1192 - 13151 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL. ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
REFER TO CHEMICAL SCREENING
CAP NOTICE

VOLUNTARY ACTIONS:
0401 IND ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER EXPOSURE
0404 LABELS/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APPLIED DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/18/92 OTS DATE: 11/02/92 CSRAD DATE: 04/20/95

CHEMICAL NAME:
Acetamide, N,N'-dimethylhydroxy-
Dimethylammonium dimethylcarbamate
Acetamide

CAS#
Unknown
Unknown
127-19-5
2155-94-4

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPICLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECOTOX/AQUA TOX	01 02 04
0221	ENV. OCCCHEM/FATE	01 02 04
0222	ENDER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQUST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METABP/HARMACO (ANIMAL)	01 02 04
0240	METABP/HARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PRODUSE/PROC	01 02 04
0251	MIXTS	01 02 04
0299	OTHER	

TRIAGE REVIEW: NON-CBI INVENTORY
YES
CAS SR
NO
IN FLAMMA

ORDERING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RAT
GP

TOXICOLOGICAL CONCERN:
LOW
MED
HIGH

USE:

PRODUCTION:

13151A

L

Dimethylammonium dimethylcarbamate: Acute oral toxicity in rats is of low concern. Single oral gavage doses to male rats were lethal at ≥2,250 mg/kg. At lethal doses, animals exhibited discomfort with labored breathing; cyanosis occurred in one rat. Necropsy revealed acute gastroenteritis at lethal doses. There were no clinical signs or pathological effects at sublethal doses.

~~M~~ L

Dimethylammonium dimethylcarbamate: Subacute oral toxicity in rats is of ~~moderate~~ low concern. Five rats received oral doses of 450 mg/kg/day for ten days. One rat was moribund on day 6. Necropsy revealed gastritis. The survivors exhibited occasional diarrhea during treatment; however, there were no associated pathological effects.

L

Dimethylammonium dimethylcarbamate: Dermal irritation in guinea pigs is of low concern. Application of the substance to the shaved skin of guinea pigs resulted in mild irritation.

L

Dimethylammonium dimethylcarbamate: Dermal sensitization in guinea pigs is of low concern. Tests for sensitization in guinea pigs were negative.

L

N,N-Dimethylacetamide: Acute oral toxicity in rats is of low concern. Single oral doses to rats were lethal at ≥7,500 mg/kg. At lethal doses, animals exhibited discomfort with labored breathing. There were no associated pathological effects.

L

N,N-Dimethylacetamide: Acute oral toxicity in guinea pigs is of low concern. Single oral doses to guinea pigs were lethal at ≥3,400 mg/kg. At lethal doses, animals exhibited discomfort with labored breathing. There were no associated pathological effects.

L

N,N-Dimethylacetamide: Subacute oral toxicity in rats is of low concern. Six male rats received oral doses of 1,500 mg/kg/day for ten days. Three animals died during the treatment. Clinical signs of toxicity included marked discomfort, irritability, pallor, weight loss, and severe diarrhea. Necropsy revealed kidney, liver, and stomach alterations.

L

N,N-Dimethylacetamide: Acute inhalation toxicity in rats is of low concern. A single 48-hour exposure to two rats at a concentration of 10,000 mg/m^3 was not lethal. There were no clinical signs of toxicity. Necropsy revealed some swelling of the cells lining the alveolar walls of the lungs.

M

N,N-Dimethylacetamide: Dermal irritation in guinea pigs is of moderate concern. Application of a 25% aqueous solution to the intact skin of guinea pigs resulted in irritation. Application of a 10% aqueous solution to the intact and abraded skin of guinea pigs resulted in temporary moderate irritation at the abraded site.

L

N,N-Dimethylacetamide: Dermal sensitization in guinea pigs is of low concern. Tests for sensitization in guinea pigs were negative.

L

N,N-Dimethylacetamide: Acute dermal toxicity in rabbits is of low concern. Single dermal doses to male rabbits were lethal at ≥5,000 mg/kg. Animals exhibited acute local inflammation of the treated area. Necropsy revealed edema and congestion of the kidney, congestion of the thymus, and congestion of the ocular blood vessels.

L

N,N-Dimethylacetamide: Subacute dermal toxicity in rabbits and rats is of low concern based on the results of two studies. In the first study, six rabbits received dermal doses of 1,000 mg/kg/day for ten days. All animals survived treatment. There were no significant clinical signs or pathological effects. In the second study, two male rats received dermal doses of 7,500 mg/kg/day. Both animals died within four treatments. Necropsy revealed liver and bone marrow damage.

L

N,N-Dimethylhydroxyacetamide: Acute oral toxicity in rats is of low concern. Single oral doses to male rats at levels up to 7,500 mg/kg were not lethal. There were no clinical signs of toxicity of pathological effects.

L

N,N-Dimethylhydroxyacetamide: Acute oral toxicity in rats is of low concern based on the results of two studies. In the first study, six rats received oral doses of 5,000 mg/kg/day. Four rats died after four treatments, and the remaining two rats were sacrificed after five treatments. Necropsy revealed signs of central nervous system stimulation (congestion and hemorrhaging of the meningeal vessels of the brain). In the second study, six rats received oral doses of 1,500 mg/kg/day for 15 days. There were no deaths or pathological effects.

L

N,N-Dimethylhydroxyacetamide: Dermal irritation in guinea pigs is of low concern. Application of a 50% aqueous solution to the intact skin of guinea pigs resulted in mild, temporary irritation.

L

N,N-Dimethylhydroxyacetamide: Dermal sensitization in guinea pigs is of low concern. Tests for

sensitization in guinea pigs were negative.

L

N,N-Dimethylallylamine: Acute oral toxicity in rats is of low concern. Single oral gavage doses to male rats were lethal at ≥1,000 mg/kg. At lethal doses, animals exhibited discomfort and labored breathing. Necropsy revealed gastroenteritis at lethal and non-lethal doses (as low as 100 mg/kg).

L

N,N-Dimethylallylamine: Subacute oral toxicity in rats is of low concern. Six rats received oral doses of 200 mg/kg/day for ten days. There were no adverse clinical signs; however, necropsy revealed gastritis.

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N,N-Dimethylallylamine: Dermal irritation in guinea pigs is of low concern. Application of a 50% aqueous solution to the intact and abraded skin of guinea pigs resulted in mild irritation.

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N,N-Dimethylallylamine: Dermal sensitization in guinea pigs is of low concern. Tests for sensitization in guinea pigs were negative.